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Systematic review on the effect of rinsing with povidone-iodine during nonsurgical periodontal therapy

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Abstract: Sahrman P, Puhan MA, Attin T, Schmidlin PR. Systematic review on the effect of rinsing with povidone-iodine during nonsurgical periodontal therapy. J Periodont Res 2009;doi: 10.1111/j.1600-0765.2009.01232.x. (c) 2009 The Authors. Journal compilation (c) 2009 Blackwell Munksgaard
Background and Objective: The existing literature is inconsistent regarding whether there is any additional effect of povidone-iodine (PVP-iodine) as an adjunctive to scaling and root planing, and, if there is an effect, what its size is. Therefore, the aim of this study was to assess the additional effect of PVP-iodine as an adjunct to scaling and root planing compared with water, saline or no rinse in the treatment of chronic periodontitis. **Material and methods:** An electronic literature search of the databases PubMed, EMBASE and the Cochrane Central Library, and a handsearch, were performed (up to November 2008). Two reviewers independently identified and selected screened abstracts for possible inclusion, and assessed randomized, controlled clinical trials comparing the additional benefit of PVP-iodine with water, saline rinsing or no rinsing in the nonsurgical periodontal therapy of patients with chronic periodontitis. **A fixed-effects meta-analysis** was conducted in the absence of statistically significant heterogeneity. **Results:** A small, but statistically significant additional beneficial effect of the adjunctive use of PVP-iodine with enhanced probing pocket depth reductions of 0.28 mm (95% confidence interval: 0.08 to 0.48, $p = 0.007$) was found. There was no significant heterogeneity between studies ($I(2) = 0\%$). However, most of the studies included in the meta-analysis were of low quality, and the treatment modalities showed various differences such as the use of PVP-iodine at different concentrations and application modalities. Nevertheless, single-rooted teeth, in particular, showed an additional benefit after scaling and root planing with PVP-iodine, particularly when the treatment was repeated during the healing stage. **Conclusion:** The adjunctive use of PVP-iodine during scaling and root planing may increase the clinical pocket depth reduction, although the clinical significance is small to moderate.

DOI: <https://doi.org/10.1111/j.1600-0765.2009.01232.x>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-31439>

Journal Article

Accepted Version

Originally published at:

Sahrman, P; Puhan, M A; Attin, T; Schmidlin, P R (2010). Systematic review on the effect of rinsing with povidone-iodine during nonsurgical periodontal therapy. Journal of Periodontal Research, 45(2):153-164.

DOI: <https://doi.org/10.1111/j.1600-0765.2009.01232.x>

Systematic review on the effect of PVP-iodine rinsing during non-surgical periodontal therapy

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Running title: "PVP-iodine in periodontal therapy"

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Keywords: Povidone-iodine, Antiseptics, Nonsurgical periodontal therapy, Pocket depth

Abstract

Objectives: To assess the additional effect of PVP-iodine as an adjunct to scaling and root planing as compared to water, saline or no rinse in the treatment of chronic periodontitis.

Background: Existing literature is inconsistent whether there is any additional effect of PVP-iodine as an adjunctive to scaling and root planing, and with the effect's size if there is one.

Methods: An electronic literature search in the databases PubMed, EMBASE, Cochrane Central Library and a handsearch were performed (up to November 2008). Two reviewers independently identified and selected screened abstracts for possible inclusion and assessed randomized, controlled clinical trials comparing the additional benefit of PVP-iodine to water or saline rinsing or no rinsing in non-surgical periodontal therapy of patients with chronic periodontitis. Fixed effects meta-analysis was conducted in the absence of statistically significant heterogeneity.

Results: A small but statistically significant additional beneficial effect of adjunctive use of PVP-iodine with enhanced probing pocket depth reductions of 0.28 mm (95% CI 0.08 to 0.48 [CI], $p=0.007$) was found. There was no significant heterogeneity between studies ($I^2=0\%$). However, most of the studies included in the meta-analysis were of low quality and the treatment modalities showed various differences like the use of PVP-iodine in different concentrations and application modalities. Nevertheless, especially single-rooted teeth showed an additional benefit after scaling and root planing with PVP-iodine, particularly when the treatment was repeated during the healing.

Conclusion: The adjunctive use of PVP-iodine during scaling and root planing may increase the clinical pocket depth reduction, although the clinical significance is small to moderate.

Introduction

Periodontitis is a common inflammatory disease of the supporting periodontal hard and soft tissues.¹⁻³ It results in a progressive destruction of the periodontal fiber apparatus and alveolar bone with subsequent apical migration of the junctional epithelium.⁴ Bacterial plaque accumulation is considered the primarily etiologic factor.^{5,6} Consequently, the aim of the therapeutical approach is the elimination of biofilm and hard deposits on the root surface. Mechanical plaque removal, using curettes and ultrasonic devices, has become a well documented and effective treatment modality.^{7,8} In addition, various attempts to eliminate pathogenic bacteria by additively administered chemical means have been explored: Systemically administered antibiotics showed significant benefits in combination with scaling and root planing⁹⁻¹³ but bear the risk of undesirable side-effects and the development of bacterial resistance.¹⁴ Topical application of antiseptics in periodontal pockets as an adjunctive to the mechanical debridement has been suggested^{15,16} and tested in various clinical trials,^{17,18} but there is still a lack of clear evidence for its additional benefit.¹⁹⁻²¹

Among these pharmaceuticals, PVP-iodine is an antiseptic with a broad antibacterial spectrum covering gram positive and negative bacteria and mycobacteria,²² *Staphylococci spp.* and *Candida albicans*²³ and periodontal pathogens.^{24,25} Several studies showed additional short-term improvements when PVP-iodine was used during subgingival debridement.²⁶⁻²⁸ Other studies failed to prove additional benefits of a PVP-iodine pocket rinsing.²⁹⁻³² This systematic review aimed to assess the potential additional effect of PVP-iodine as an adjunct to scaling and root planing as compared to water, saline or no rinse in the treatment of chronic periodontitis.

Material and methods

Search strategy

In order to systematically review the data published on the subject of interest, a literature search in the *U.S. National Library of Medicine (Pubmed)*, *Excerpta Medical Database (Embase)* and the *Cochrane Central Library* was performed. Articles from

inception of these databases up to and including November 2008 were considered.

The following search terms were used:

(PVP-iodine) OR (iodine) OR (PVP) OR (povidone)

AND

(periodontitis) OR (periodontal)

including the according MeSH terms, respectively.

A manual search included the reference list of the reviews and studies concerning the topic as well as the index of context of the Journal of Clinical Periodontology, Journal of Periodontal Research and Journal of Periodontology.

Study selection

In a first step, the two reviewers (PS, PRS) independently screened titles and abstracts of the electronic search and assessed them for possible inclusion in the review. We ordered all potentially eligible studies and assessed their full texts. We did not apply any language restrictions

Any disagreement concerning inclusion was resolved by discussion.

Eligibility criteria for studies

We included randomized, controlled clinical trials comparing the additional benefit of PVP-iodine to water or saline rinsing or no rinsing in non-surgical periodontal therapy in patients with chronic periodontitis. Only studies reporting on the therapy of chronic periodontitis in otherwise healthy adults were included. Consequently, studies with treatment of aggressive periodontitis, treatment of non-adults and patients with systemic diseases or manifestations affecting the prognosis and therapy of periodontitis (e.g. diabetic, pregnant or HIV-positive patients) were excluded.

With regard to the instrumentation the use of either hand curettes or ultrasonic devices were included. Only sole non-surgical techniques were considered.

Our primary outcome was the periodontal probing depth (PPD) after three months and at final follow-up. Secondary outcomes included indices for clinical attachment loss (CAL), oral hygiene and gingival bleeding.

Data extraction and quality assessment

The reviewers (PS, PRS) independently extracted the following data: Bibliographic details, patient characteristics, description of the interventions and types of outcomes. Whenever possible, we extracted mean baseline and follow-up values (including standard deviations) for each treatment group as well as differences between groups and corresponding measures for precision (standard errors, 95% confidence intervals [CI]). The reviewers independently assessed the quality of included trials by evaluating whether the method of randomization was valid, whether there was concealment of random allocation and whether patients and examiners were masked. Again, any discrepancies for data extraction and quality assessment were resolved by consensus.

Data analysis

We expressed treatment effects as mean differences in mm in PPD and corresponding 95% CI. We pooled data across studies in absence of significant heterogeneity ($p > 0.1$ for χ^2) using fixed effects (inverse variance method) and random effects (DerSimonian-Laird method) models. Since the results from fixed and random effects models were identical, we only reported the fixed effects models. Heterogeneity was assessed using χ^2 statistic and the proportion of variation due to heterogeneity was expressed as I^2 . In the absence of a clear definition of what constitutes a clinically relevant effect we considered a Cohen's effect size ($d = \frac{\text{mean value}}{\text{standard deviation}}$) ³³ of 0.2 to represent a small and 0.5 a moderate effect. We conducted all analyses with STATA for windows version 10.0 (Stata Corp; College Station, TX).

Results

Search and screening

From initially 186 titles from the literature search 32 full texts were assessed separately and independently by both reviewers for possible inclusion in the review (Figure 1). Twenty-five articles were excluded for the following reasons (Table 1): no scaling and root planing conducted or additional surgery (9 studies), disinfection

protocol without PVP-iodine (8 studies), no assessment or presentation of clinical parameters (3 studies), missing control group or randomization (3 studies) or additional use of antibiotics (2 studies). Reviewers agreed in 96.7% (30/31 studies) about in- and exclusion and resolved disagreement for one paper by discussion.

From the remaining 7 original articles^{26-30,32} the data for the assessment parameters and any available information on randomisation method, concealment and blinding were extracted. These studies included data of 424 patients (Table 2).

Description of studies

Five of the seven studies included in the review were designed as parallel studies,^{26,27,29,30,32} two as split mouth studies.^{28,31}

Due to different inclusion criteria the investigated teeth varied in number of roots, pocket locations like possible assessment of furcation sites and finally pocket depths across studies (Table 3). Baseline values for probing depths varied from $3.9 \pm 0.9\text{mm}$ ¹⁵ to $\geq 6\text{mm}$.^{28,31}

The patient populations varied by means of explicit exclusion of smokers in four studies,^{27,29-31} and the exclusive treatment of single-rooted¹⁵ or non-molar teeth only.

³¹ The majority of the publications reported oral hygiene instructions,^{15,29-32} and three of them included supragingival scaling and removal of plaque retentive factors.³⁰⁻³²

The concentration of PVP-iodine used for treatment ranged from 0.1% to 10%. The individual studies reported on different recall intervals and study periods. The shortest reevaluation periods ranged from one month to 5 weeks, but most studies covered data for several times of reinvestigation. Aside the comparison of the final results at the end of the investigation periods an analysis after a collective observation period was made: Three studies reported evaluable values for probing depth at three months after intervention (Figure 2).^{26,27,32}

One study²⁶ included nearly one half of the over-all patient population (see table 2).

Quality assessment

Six of seven studies²⁷⁻³² reported to be randomized trials (Table 4). For one trial,²⁶ uncertainty remained but the authors of that study confirmed randomization upon contacting them. 29% of the studies described their methods of randomization,^{29,30} 43% the concealment of random allocation^{28,29,31} and 57% gave information about the

methodology of “blinding” or “masking” of the examiner^{27,29,31,32} (Table 2).

Effects of additional rinsing with PVP-iodine on PPD

We could not include one of the seven trials into the meta-analyses because data were not fully reported.³¹ In all studies, the mean values for the PPD of control and test sites at baseline were similar. They ranged between 3.9 ± 0.9 mm and 5.96 ± 1.16 mm. After 3 months the PPD values ranged between 2.7 mm and 4.0 mm for the test sites and 2.9 mm and 4.5 mm for the control sites (Figure 2, Table 6).

The meta-analyses at the studies' end of follow-up showed a statistically significant additional effect of PVP-iodine with regard to PPD change of 0.28 mm (95% CI 0.08-0.48) ($p=0.007$, Figure 3). Effect size indices ranged from 0.2 to 0.48.

For the three month follow up the additional effect for PVP-iodine in the meta-analysis for three evaluable studies is 0.23 mm (95% CI -0.03, 0.48) (Figure 2).

Table 2 shows the data according to the number of patients. An analysis based on the number of pockets was statistically not possible since we could not account for the within person variability when more than one pocket was treated.

Effects of iodine on secondary outcomes

Table 7 shows how attachment levels changed from baseline to the 3-months follow-up and to final follow-up. At the end of the studies, the differences between test and control groups in attachment level changes ranged from -0.13 mm (altogether two studies favouring the control group) to 0.95 mm (with four studies favouring the test group). Values for the plaque index and BoP are given in Table 8 and 9. The mean values of the plaque index varied at baseline between 3.9%-61% and were reduced equally for test and control sites. Bleeding-on-probing scores of initially 27 to 80% dropped without remarkable differences for both groups.

Discussion

PVP-iodine as an antiseptic adjunctive during non-surgical periodontitis therapy has been used in various studies - but with inconsistent results.^{26-32,34} Comparing six studies in a meta-analysis, this systematic review showed a small but statistically significant effect of additional PVP-iodine rinsing during deep scaling and root planing

with regard to reduction in PPD in patients with chronic periodontitis. In the three month's meta-analysis the effect was less pronounced. The results published for clinical attachment gain (Table 7) support the findings for the probing depth (Table 7). Equally distributed values for the oral hygiene indices PI and BOP proved similar oral hygiene levels in control and treatment groups.

This systematic review was performed strictly following the guidelines and recommendations of the QUOROM statement for meta-analyses.³⁵

However, it was not possible to contact the authors of all included studies to get more detailed data, which would have been helpful especially in the case of the Leonhardt study,³¹ which had to be excluded from the meta-analysis due to insufficient data reporting of probing depth. Also, the studies included in this review were of low to moderate quality according to the classification of Schulz (Table 2).³⁶ The latter overview showed that studies, which do not report the sensitive details of subverting the purpose of randomization and allocation concealment have been associated with larger treatment effects.

We observed little heterogeneity ($I^2=0$) across studies: Initial probing depths of intervention and control groups were similar, and the pocket depth reduction in the control groups from 0.8 mm (for pockets with initially 3.9 ± 0.9 mm)²⁶ to 2.31 mm (from initially 5.96 ± 1.16 mm)³⁰ ranged in the accepted interval published in the existing literature.^{24,37}

Effect sizes for additional rinsing with PVP-iodine were between 0.2 and 0.48 and, according to Cohen's effect size³³, small (≥ 0.2) to moderate (≥ 0.5). Indirectly comparing the adjunctive use of PVP-iodine to other additional treatment types it is likely to be similarly effective as the systemic administration of the antibiotic spiramycin (additional probing depth reduction 0.3 mm)^{10,38,39} or a full mouth disinfection regimen in single rooted teeth (additional probing depth reduction 0.3 mm).^{40,41}

However, the results of the individual studies were inconsistent. Two different reasons for this must be taken into consideration:

First, the two studies supporting an overall favorable effect of PVP-iodine usage^{26,27} investigated single-rooted teeth while two of the studies with a less favorable outcome^{30,32} explicitly referred to multi-rooted teeth. Notably, one of the latter studies found a statistically significant additional benefit for PVP-iodine at the deep sites for

all reevaluation times.³⁰ Another study that investigated the effect of PVP-iodine during scaling and root planing on single-rooted teeth was excluded from the review due to missing randomization, but also confirmed an additional benefit for this antiseptic.³⁴ The conclusion of this comparison is, that the treatment of single-rooted teeth with PVP-iodine might result in a more pronounced additional probing depth reduction than the overall results.

A second aspect is, that the two studies that showed an additional benefit for PVP-iodine use^{26,27} had another relevant fact in common: both studies reported a second scaling and root planing of the test and control teeth with or without the use of PVP-iodine after one month²⁷ or three to four months after the first intervention.²⁶

Likewise, a second scaling was performed after three months by Del Peloso Ribeiro and co-workers favoring the results for PVP-iodine in deep pockets.³⁰ Therefore, a second scaling and root planing after at least one month after the first instrumentation, seems to result in a significant additional pocket depth reduction potential if PVP-iodine is used, compared to a water or saline rinse. This finding corresponds well with investigations demonstrating recolonization of the periodontal pocket between four⁴² and nine weeks⁴³ after scaling and root planing, that is successively followed by a re-deepening of the periodontal pockets.

Interestingly, no correlation between the concentrations of the PVP-iodine used in the studies and the additional benefit in PPD was found. Furthermore, no correlation was found for the contact time. This finding conflicts with an assumption of a previous review on the effect of PVP-iodine: Concentration and contact time were suspected as the crucial parameters for success with the iodine rinse.⁴⁴ Independence of the results from concentration are consistent with findings stating that PVP-iodine has its maximum bactericide concentration at a low level of 0.1%⁴⁴ due to a higher disposability of the iodine in the PVP complex.⁴⁵ Once applied into the pockets higher concentrated preparations get diluted by gingival crevicular fluid and blood, until a low concentration of 0.1% is presumably reached.

The exclusion of smokers in some studies did not result in different outcomes in pocket depth reductions: Even in studies excluding smokers^{27,29,30} the results were discordant about an additional benefit of PVP-iodine use.

In the examined publications for this review we could not find any reported adverse effects on PVP-iodine. Though there are dermatological studies that indicate skin

irritations after long-term use of PVP-iodine, ⁴⁶ adverse effects for this antiseptic are considered rare and nonserious.⁴⁷ Furthermore, there are no bacterial resistances against PVP-iodine.^{23,48,49} Chairside application of PVP-iodine does not cause an enduring staining of the dental soft and hard tissues. Displeasing staining of clothing and the dental unit may easily be removed by the application of an aqueous solution of sodium thiosulphate.

Nevertheless, the topical application of PVP-iodine during non-surgical scaling and root planing seems a promising way to improve clinical outcomes. However, further clinical studies with PVP-iodine are needed to investigate and to improve its beneficial effect in the therapy of periodontitis: Firstly, this review indicated that the assumption that concentration is a key parameter for povidone's effectiveness could not be verified. Secondly, investigations with a very similar studies design are discordant about if there really *is* an additional effect when PVP-iodine is used and if there is about its *extent*. Thirdly, the results of this review are limited on the data of not more than six RCT-studies. Subsequently, we need clinical studies that investigate treatment variations like repeated applications to render the additional benefit of the cheap and nonhazardous broadband antiseptic PVP-iodine predictable. Furthermore, the effect of repeated rinsing or the application of PVP-iodine in a pharmaceutical form with a higher substantivity should be investigated.

Conclusion: The adjunctive use of PVP-iodine during scaling and root planing significantly increased clinical pocket depth reduction although the clinical significance was still small.

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Figure legends:

Figure 1: Screening method

*Figure 2: Studies investigating an additional effect of PVP-iodine
(three month after intervention)*

Figure 3: Studies investigating an additional effect of PVP-iodine (studies' end)

Table legends:

Table 1. Excluded studies

Table 2: Data sources for weighting of the studies

Table 3: Description of studies

Table 4: Quality assessment

Table 5: Development of Probing Depth: Total investigation period

Table 6: Development of probing depth: At three month of observation period

Table 7: Development of attachment level

Table 8: Development of the plaque index

Table 9: Development of bleeding-on-probing

Table 3: Description of studies

Author, year of publication	Population	Treatment prior to intervention	Intervention test/control	Intervention	Control	Parameter assessment	Investigation period	maintenance
Rosling 01	N=223 (9/31 excluded=losers, advanced perio, healthy, min 8 non-molar-teeth, ppd≥6mm at ≥2 teeth/each quadrant, rx bone removed loss≥40%	Case presentation, oral hygiene instruction, „hopeless“ teeth	US-Sc (Odontoson), (local anesthesia) 4-6 60min-visits within 1 week	PVP-iodine 0,1%	Tap water	PPD (6 sites/tooth, PCP15) AL Plaque Index BoP Gingival Index Radiological bone hight	12m	Supportive Periodontal Treatment every 3-4 months including ScPr at PPD≥5mm with/without iodine, Recall 3m, 6m, 12m, after 3a, 5a, 13a (maintenance)
			<i>Parallel design</i>			After 3, 6, 12 m, annually		
Hoang 03	N=16 (3 diabetes II, 1 psychiatric, 1 down), [26,73a] ≥1 pocket ≥6mm/each quadrant, 1 Pocket t/c 7/9 m/f	Mb-testing, oral hygiene instruction	ScRp with hand currettes (loc. anesthesia) ≥2h	PVP-iodine 10% repeated irrigations for 5min	Sterile saline	PPD (6 sites/tooth, manual) Plaque Index BoP Microbial testing	5w	Microbial testing, ScRp except test/control-teeth (5w)
			<i>Split mouth design</i>			5w		
Koshy 05	N=36, [34-66a], ≥2pockets≥5mm, non smokers, moderate-to-advanced chronic periodontitis 13/23 m/f	1-2x tooth-brushing visits incl id	Single-visit US-Sc supra and subgingival (PiezonMaster 400 EMS/Perio slim tip) (loc. anesthesia)	PVP-iodine 1%	Destilled water	PPD (6 sites/tooth, PCP15) AL Plaque Index BoP Mobility	6m	test-group: 0,05% CHX mouthwash 2x/d, tongue-brushing, oral hygiene remotivation +professional tooth cleaning 1x/m without US
			<i>Parallel design</i>			At 1m, 3m, 6m		
Del Peloso Ribeiro 06	N=48 (4 fall-outs)) healthy nonsmokers Chronic periodontitis with Class II+III Furcation ,BoP+, ≥1 tooth withPD≥5mm 20/24 m/f	Oral hygiene motivation, information about etiology, removal of plaque retentive factors	Subgingival instrumentation with ultrasonic device (Loc. anesthesia)	PVP-iodine 10%	Destilled water	PPD (1 site/tooth, PCP15, stents) At 1m, 3m, 6m	6m	Professional supragingival plaque control, oral hygiene instruction every 15d (1st m) then once/m At 3m: subging ScRp
			<i>Parallel design</i>					
Leonhardt 06	N=20 [39-68a], advanced perio, at least 1 single-rooted with at least 1 PD≥6mm, BoP+, non-smokers 8/12 m/f	Information about periodontal condition, supraging sc, hygiene instruction for one month brushing/id, when PI≤15% treatment start	US-Sc Odontogain (loc anesthesia) 4min/tooth by a dental hygienist	PVP-iodine 0,5% for 5min/tooth	Sterile saline-solution for 5min/tooth	PPD (6 sites/tooth, PCP15) Plaque Index BoP at 6m	6m	-
			<i>Split mouth design</i>					
Forabosco 06	N=60 with adult periodontitis, - [35-65a], non-smokers (since at least 5 y), PD≥5mm at monoradicular teeth, BoP+, at 7 teeth or more 25/35 m/f		ScRp	Odontoson + PVP-iodine 10%	Odontoson+ NaCl(20)	PPD (manual) AL BoP Mobility At 1m, 3m, 4m	4m	Group specific ScRp with/without PVP-iodine after 1 m
			<i>Parallel design</i>					

Zanatta 06	N=45 (5 drop-out: 3 losers≥2mm), advanced chronic perio, ≥8 teeth with PPD ≥5mm, BoP+ 27m, 18w	Removal of supragingival plaque retention factors, filling of cavities	ultrasonic debridement: 45min full-mouth	PVP-iodine 0,5%	0,9% NaCl	PPD (6 sites/tooth, PCP15) CAL Plaque Index BoP Recession	3m	Oral antiseptics interdicted, clinical parameters 2 weeks following initial treatment, at 1m, 3m
<i>Parallel design</i>						At 3m		
<i>m/f – ratio males/females</i>	<i>id – interdental</i>	<i>ScRp – Scaling and Rootplaning</i>	<i>PPD – Periodontal Probing Depth</i>	<i>BoP – Bleeding on Probing</i>	<i>AL – Attachment level</i>	<i>US – ultrasonic device</i>		